Editorial

Pandemic 2009–2010 influenza vaccine: Six lessons learned and the way forward (Allegro not Adagio)

In June 2009 the WHO declared the first influenza pandemic of the 21st century. At least two waves of the pandemic were discernible – a Spring 2009 wave, and a Fall-Winter 2010 wave. Now that the second wave of the pandemic has subsided, it is appropriate to look back and begin to ask questions that might inform future pandemic vaccine response efforts.

It appears that the first cases of influenza-like respiratory illnesses occurred in Mexico in the late February-early March 2009 timeframe. Mexican public health authorities investigated the outbreaks of respiratory illness, but lacked definitive laboratory confirmation of the responsible pathogen. The US Department of Defense (DoD), conducting research on respiratory diseases at the US–Mexico border identified the first two unrelated cases of novel influenza A/H1N1 (later termed A/California/H1N1), as did the US Centers for Control and Prevention.

By May, the decision was made to embark on manufacture of a monovalent vaccine to protect against A/California/H1N1. The US Food and Drug Administration (FDA) ruled that vaccine development could proceed along the regulatory pathway approved for seasonal influenza vaccines as a simple strain change. This meant that only manufacturers already FDA-approved for production and marketing of seasonal influenza vaccines could produce such vaccines (at least for use in the US), and only in facilities FDA-approved for manufacture using only identical methods approved by FDA. As a result, five manufacturers were eligible to produce vaccine – GlaxoSmithKline, Sanofi Pasteur, MedImmune, CSL, and Novartis. In addition, the decision was made that the US government would purchase all doses used in the US, and vaccine would be distributed, based on population, to individual states through state public health programs.

Unfortunately, given the limitations of egg-based vaccine manufacture, and as predicted by several vaccine experts, almost immediately problems began to arise. It took weeks before an adequately high-growth egg-adapted reassortant strain could be produced and distributed to manufacturers. Several manufacturers identified difficulties in viral yields, and struggled to maximize output. As a result, vaccine manufacture and delivery was slower than anticipated. Unfortunately, many throughout government and in academia were overly optimistic about the amount and timing of vaccine availability and distribution. Repeated DHHS, BARDA, CDC, and many in pharma and academia provided repeated assurances of accelerated vaccine availability – which, unfortunately had no basis in fact given the realities of current influenza vaccine manufacturing technology. As a result, vaccine did not start to become available until mid- to late-October, which was the peak of the second wave of pandemic cases, making the vaccine “too little, too late”. The net result were reactions among providers and the public of two extremes – one group convinced the vaccine was “rushed” and inadequately tested for safety, and a second group angry and frustrated that vaccine was unavailable. This created a sense of confusion, and mistrust that the authorities knew what they were doing.

Further problems arose in regards to establishing priority groups for vaccination. An initial set of risk-based groups was established in the US, but this totaled almost 150 million persons (half of the US population), and almost immediately had to be modified to prioritize a smaller group of roughly 40 million persons, consistent with vaccine availability. This too, contributed to confusion and a sense of mistrust.

The sad result, and not unexpectedly, was that significant numbers of the public, and even HCWs, opposed receipt of the vaccine fearing that it was a “new” vaccine, untested, “rushed to market”, and perhaps unsafe. As a result only an estimated 37% of US HCWs received H1N1 vaccine, and only 34% of them received both monovalent H1N1 and trivalent seasonal influenza vaccine during 2009–2010 [1]. In turn, this undoubtedly influenced their willingness to educate and offer vaccine to their patients. As a result, vaccination coverage rates among the public was spotty, and under-utilized, particularly among infants and children.

Below I catalog lessons learned from the 2009–2010 pandemic, specifically in terms of the vaccine aspects of public health response, and discuss how such issues might be addressed:

1. Having a pandemic plan is critical to rapid and effective response, and served the United States and other prepared countries well. Significant plans for response had been developed at the US Federal and state-levels, in Canada, and in most major Western European and Asian countries. Unfortunately, according to the WHO, far fewer countries had developed comprehensive pandemic response plans.

2. For the US, the major issue in responding to the pandemic was reliance on influenza vaccine manufacturing technology that has inherent limitations in terms of the amount of time necessary to prepare vaccine. Our ability to produce and deliver influenza vaccines are not markedly different from that used over the last 50 years, and is simply a function of the time needed for egg-based vaccine manufacture. Thus, a major lesson learned is that we must develop, and implement, a variety of innovative solutions toward the need to accelerate new technologies for vaccine manufacture. Part of the solution must be investment by both...
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pharma, and incentives provided by government, and indeed such progress is apparent in the case of mammalian cell-based manufacture. But such progress must be accelerated, and in partnership with regulatory agencies, innovative and unconvincing new licensure pathways developed. Our improved surveillance abilities are paradoxically likely to exacerbate the public’s frustration with the time interval from discovery of a pandemic threat, and the ability to be protected by vaccine, as we recognize pandemic threat much sooner than we did 50 years ago. Numerous clinical studies and reviews have outlined new methods for rapidly producing vaccine, new adjuvants, and new methods for antigen-sparing; and will not be reviewed here. Further research and movement of new products into the market are appropriate and need to be incentivized.

3. Accurate and regularly updated vaccine availability announcements are critical to engaging the public and providers, and in developing trust in authorities. Promising vaccine availability sooner than is likely is counterproductive and diminished trust that the authorities knew what they were doing.

4. Greater efforts at educating the public and providers about influenza vaccine safety and manufacture represents a critical pathway in effective public health response. As noted above, both the public and providers remained unconvinced of the safety of the vaccine – despite traditional methods of education. Had the pandemic been more morbid than it was, our ability to mount an effective response in terms of having healthy HCWs present at work, would have been heavily compromised as they themselves developed illness. Continuing medical education, certification review courses and exams, and other means must be utilized in order to teach physicians, nurses, pharmacists, and others accurate scientific information about influenza vaccines and their use as an individual and public health response issue. A separate issue is the need for requirements for HCWs to receive vaccine as called for by IDSA, SHEA, APIC, NFID, AMA, ACP, APA, and the NPSF.

5. Faster and more consistent vaccine distribution methods are the final common critical pathway in pandemic response efforts and represent an area for additional research and program management. Distribution through state public health offices was uneven. Optimal methods for vaccine distribution must be determined that take into account the unpredictable timing of pandemics (with decades between intervening pandemics), public health staffing and budget issues, as well as addressing other day-to-day issues such as maintaining personnel training and the ability to storehouse vaccines; if we are to do better next time. In this regard, expert groups examining these issues could profitably be convened such as the Council for State and Territorial Epidemiologists or a similar body of those actually involved in distributing vaccines.

6. Streamlining the plan. Specific workgroups of appropriate experts, to include those at the distribution and provider level, state and local public health officials, and others should be constituted and charged with critically evaluating the US pandemic response in each of its dimensions; with the goal of improving, refining, and designing a new doctrine and plan for response. Such efforts are already underway. Similarly, public health efforts such as pandemic response are most effective when practiced as a global community. WHO should convene meetings designed to critically evaluate pandemic responses by country and by region, and from the derived “lessons learned” develop new pandemic response doctrines.

The 2009–2010 influenza pandemic may have led to as many as 44,000 deaths, and 2 million years of life lost just in the US alone [2]. The average age of its victims was 37 years; compared to 76 years for seasonal influenza outbreaks. Many of us are aware of how strikingly worse the outcome could have been had the virus been truly novel, highly transmissible, and more pathogenic that it was. Our ability to quickly manufacture and distribute vaccine was hampered by technology with inherent time limitations, and from the point of view of vaccine, was “too little too late.” While certainly not the fault of any individual or group, collectively we all share guilt in not more vigorously insisting on 21st century methods of vaccine production, and industry-standard rapid distribution and inventory methods for delivering life-saving vaccines to the public.

Perhaps most striking was the chasm between HCWs who for the most part believed the vaccine to be safe, and on the other hand, by those HCWs who professed concerns about vaccine safety. For the latter group, this was directly reflected in their refusal to themselves be immunized, and almost certainly contributed to decreased uptake of the vaccine by the public they serve. We must do better, and since 1997 with the initial identification of influenza A/H5N1, we have thus far been given almost 14 years warning regarding the need to be better prepared. We had best do so.

References


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